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(51) International Patent Classification⁶ : C12N 15/62, C07K 19/00, 14/82, 14/52, 14/78, 14/47, 16/18, 16/28, 16/44, C12N M1, 1/19, 5/10, A61K 38/17, 39/395, G01N 33/50 // (C12N 1/21, C12R 1:19)	A3	(11) International Publication Number: WO 96137621 (43) International Publication Date: 28 November 1996 (28.11.96)
(21) International Application Number: PCT/EP96/02230 (22) International Filing Date: 23 May 1996 (23.05.96) (30) Priority Data: 95107914.4 23 May 1995 (23.05.95) EP (34) Countries for which the regional or international application was filed: DE et al. (71) Applicant (for all designated States except US): MORPHOSYS GESELLSCHAFT FÜR PROTEINOPTIMIERUNG MBH [DWDE]; Frankfurter Ring 193a, D-80807 Munich (DE). (72) Inventors; and (75) Inventors/Applicants (for US only): PACK, Peter [DWDE]; Franz-Wolter-Strasse 4/III, D-81925 Oberföhring (DE). HOESS, Adolf [DWDE]; Wirtsbreite 21, D-83672 Wangau (DE). (74) Agent: VOSSIUS AND PARTNER; P.O. Box 86 07 67, D-81634 München (DE).	(81) Designated States: CA, CN, JP, US, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments. (88) Date of publication of the international search report: 3 January 1997 (03.01.97)	
(54) Title: MULTIMERIC PROTEINS (57) Abstract <p>The present invention relates to the construction and use of small multimerization devices, preferably of human origin, which self-assemble fused functional domains to multimeric and multifunctional complexes. Multimerization devices of this invention do not significantly interfere with secretion, expression yields and the independent folding of functional domains, which are attached via flexible but protease-resistant linkers. Modular gene cassettes encoding functional domains, linkers and multimerization domain can easily be combined to a cistron encoding the multimeric protein. Translation in a suitable host results in self-assembly to multimers larger than dimers. In cases, in which one or both functional domains are not expressible in sufficient yields or native fold in the same expression host, multimeric proteins can be produced, in which one or both functional domains or the multimerization device are produced separately by, e.g., in vitro translation, peptide synthesis and/or refolding and subsequently, e.g., chemically coupled to the remaining part of the multimeric protein.</p>		

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INTERNATIONAL SEARCH REPORT

Int. l. Application No

PCT/EP 96/02230

4. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/62 C07K19/00 C07K14/82 C07K14/52 C07K14/78
 C07K14/47 C07K16/18 C07K16/44 C07K16/28 C12N1/21
 C12N1/19 C12N5/10 A61K38/17 A61K39/395 G01N33/50

According to International Patent Classification (IPC) or to both national classification and IPC

3. FIELDS SEARCHED

Minimum documentations searched (classification system followed by classification symbols)

IPC 6 C12N C07K A61K G01N

Documentations searched other than minimum documentations to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO, A, 96 13583 (MORPHOSYS PROTEINOPTIMIERUNG ; PACK PETER (DE) ; LUPAS ANDREI (DE)) 9 May 1996 see figure 2 ---	1,25-37
X	J IMMUNOL METHODS, JAN 27 1995, 178 (2) P201-9, NETHERLANDS, XP000608189 DUBEL S ET AL: "Bifunctional and multimeric complexes of streptavidin fused to single chain antibodies (scFv)." see the whole document --- -/--	1,25-41

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Date of the actual completion of the international search

5 November 1996

Date of mailing of the international search report

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International Application No PCT/EP 96/02230					
A. CLASSIFICATION OF SUBJECT MATTER IPC 6 // (C12N1/21, C12R1:19)					
Accordine to International Patent Classification (IPC) or to both national classification and IPC					
B. FIELDS SEARCHED Minimum documentahon searched (classification system followed by classification symbols)					
Documentation searched other than minimum documentahon to the extent that such documents are included in the fields searched					
Electronic data base consulted during the international search (name of data base and, where prachcal, search terms used)					
Category *	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 15%; padding: 5px;">Citation of document, with indication, where appropriate, of the relevant passages</th> <th style="width: 15%; padding: 5px;">Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td style="padding: 5px; vertical-align: top;"> P,X HUM ANTIBODIES HYBRIDOMAS, 1995, 6 (3) P93-101, UNITED STATES, XP000607119 KIPRIYANOV SM ET AL: "Single-chain antibody streptavidin fusions: tetrameric bifunctional scFv-complexes with biotin binding activity and enhanced affinity to antigen." see figure 5 --- WO,A,93 15210 (MERCK PATENT GMBH) 5 August 1993 cited in the application see page 10 - page 13; examples 1-4 --- -/-- </td> <td style="padding: 5px; vertical-align: top; text-align: center;"> 1,25-41 1-3, 12-16, 25-41 </td> </tr> </tbody> </table>	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	P,X HUM ANTIBODIES HYBRIDOMAS, 1995, 6 (3) P93-101, UNITED STATES, XP000607119 KIPRIYANOV SM ET AL: "Single-chain antibody streptavidin fusions: tetrameric bifunctional scFv-complexes with biotin binding activity and enhanced affinity to antigen." see figure 5 --- WO,A,93 15210 (MERCK PATENT GMBH) 5 August 1993 cited in the application see page 10 - page 13; examples 1-4 --- -/--	1,25-41 1-3, 12-16, 25-41
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Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Y	FEBS LETTERS, vol. 341, 1994, AMSTERDAM NL, pages 54-58, XP002017642 EFIMOV VP ET AL: "The thrombospondin-like chains of cartilage oligomeric matrix protein are assembled by a five-stranded alpha-helical bundle between residues 20 and 83" cited in the application see the whole document ---	1-7, 12-16, 25-41
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Y	SCIENCE, MAR 10 1995, 267 (5203) P1498-502, UNITED STATES, XP000608194 JEFFREY PD ET AL: "Crystal structure of the tetramerization domain of the p53 tumor suppressor at 1.7 angstroms." cited in the application see abstract -----	1-3, 12-16, 25-41

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Information on patent family members

International Application No

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